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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/553,969 | 04/21/2000 | Donald G. Wallace | 17067-002040 | 6560 |

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| EXAMINER | |
|---|---|
| CHANNAVAJJALA, LAKSHMI SARADA | |
| ART UNIT | PAPER NUMBER |
| 1611 | |

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| 11/25/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/553,969 | WALLACE ET AL. | |
| | Examiner | Art Unit | |
| | Lakshmi S. Channavajjala | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,19,21,24-27,29-32 and 34-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 19, 21, 24-27, 29-32 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-17-09;7-15-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Receipt of response dated 7-29-08 and IDS dated 9-17-09 and 7-15-09 is acknowledged.

Claims 2-18, 20, 22-23, 28 and 33 have been canceled.

Claims 1, 19, 21, 24-27, 29-32 and 34-36 are pending in the instant application.

In response to the amendment to claim 30 and the persuasive argument with respect to the objection of claim 36, the following rejection has been withdrawn:

Claim 30 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Instant claim 30 is dependent from claim 1, which is limited to an aqueous colloid being a protein. Instant claim now recites that the aqueous colloid is a polysaccharide, which contradicts claim 1.

Claim 36 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 31. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 36 recites the same features as the dependent claim 31, which incorporates all the limitations of claim 1 and also the additional limitation of a non-biological polymer.

The following rejection of record has been maintained:

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 1, 19, 21, 24, 29 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,482,386 to Wittwer et al (Wittwer).**

Wittwer et al teach conditioned water-swellable hydrocolloids for use in mechanical forming processes such as processes such as die molding or injection molding in preparing shaped articles (abstract, col. 10 and col. 2, L 66 through col. 3, l 13). Wittwer teaches a number of polymers such as protein or non-biological polymers for preparing swellable hydrocolloids including gelatin (col. 2, L 37-57). Example in col. 4 describes the preparation of gelating preparation, where in gelatin is conditioned or hydrated to 15% water content and the gelating granules. Further, Wittwer teaches that gelatin is in a granulated form with a mean particle diameter of 0.2 to 4 mm. (claim 6). With respect to the degradation claimed, the property of degradation is associated with gelatin. Wittwer does not teach the hydrocolloid in an applicator but suggests that the granulated gelatin is coupled with a molding unit such as an injection molding machine and therefore the claimed hydrogel being in an applicator with an extrusion orifice so as to be able to inject gelatin hydrocolloid would have been within the scope of a skilled artisan. Even though Wittwer fails to exemplify other swellable polymers, it would have

been obvious for a skilled artisan to choose a biological polymer such as protein or a non-biological polymer or a synthetic polymer to prepare swellable hydrocolloids because Wittwer suggests that the process of preparing a swellable hydrocolloids of predetermined water content, that are suitable for preparing moldable or shaped articles can also be prepared with synthetic polymers.

***Response to Arguments***

Applicant's arguments filed 7-29-09 have been fully considered but they are not persuasive.

Applicants argue that it appears therefore that the obviousness rejection is based on the "obvious to try" rationale. According to this rationale, it is obvious to choose from a finite number of predictable solutions when solving a recognized problem. It is argued that Office Action does not establish that there had been a finite number of identified predictable potential solutions as required by KSR at 1397. It is argued that to the contrary, at col. 2 lines 49-60, Wittwer states that the hydrophilic polymer may be modified by crosslinking agents such as salts or tri or tetravalent metals, aldehydes, dialdehydes, halogenated aldehydes, mucochloric acid, 1,1- and 1-4 diketones, quinones, acid anhydrides, vinylsulfones, acrylamides, products with 3-membered rings such as ethyleneoxide or ethyleneimine, carbamoylonium compounds, etc., and that by such crosslinking agents the water-swellability can be varied within wide limits. Applicants' argue that Wittwer's list of crosslinking agents is admittedly incomplete by use of the term etcetera, and thus Wittwer cannot be used to establish that there were a finite number of solutions to obtain the presently claimed equilibrium swells. Moreover,

assuming for the sake of argument that Wittwer did establish a finite number of solutions (which it did not), Wittwer does not establish that such a finite number of solutions were also identified and predictable solutions, as required by the "obvious to try" rationale.

It is argued that Wittwer describes a water-swellable hydrocolloid, varying water swellability with certain limits. It is argued that the absorption isotherm (fig. 1) shows water content that is 0.0 to 0.5 kg water per kg gelatin. It is argued that Wittwer does not even remotely contemplate the presently claimed equilibrium swells. As indicated in the instant application at, for example, page 18 lines 17-28, the term "equilibrium swell" can be defined as the percent swell at equilibrium, and the term "percent swell" can be defined as the dry weight subtracted from the wet weight, divided by the dry weight and multiplied by 100. According to this construction, Wittwer's maximum water content of about 0.5 involves a dry weight of 1.0kg and a wet weight of 1.5kg. Hence, Wittwer's resulting maximum percentage is ((1.5-1)/1)*(100) = 50%. Wittwer's 50% value relates to water content, but Wittwer does not mention equilibrium swell value ranges at all. Thus, it is argued that although Wittwer may discuss water content or varying the water swellability, Wittwer does not teach or suggest equilibrium swells from 400% to 5000% as presently claimed. Hence, it is argued that the artisan would not be able to produce gelatin hydrocolloid gels with the desired amount of water and obtain an even distribution of water within the granules.

Applicants' arguments are not persuasive because applicants rightly pointed out that Wittwer does suggest obtaining equilibrium swell, avoid rapid degradation and

maintain water content. Even though Wittwer teaches a finite number of crosslinking agents (which may be incomplete according to applicants), the burden is on applicants to show that the finite and incomplete list of crosslinkers of Wittwer do not provide an equilibrium swell anywhere between 400% to 5000%, even though the reference desires to provide an equilibrium swell that is variable. As explained in the previous action, Wittwer's disclosure is concerned with water-swellable hydrocolloid and particularly, the product applied for injection molding in a swellable state. Additionally, Wittwer suggests varying water swellability (col. 2, l 57-60) and also suggests obtaining particles with higher water content (col. 3, L 11). Wittwer suggests that to produce shaped articles with swellable hydrocolloids, the materials need to be plasticized and that plasticity of such water swellable colloids is a function of temperature (col. 1). Wittwer also states that swellability is also a function of the granularity and specific surface of the material and further suggests optimizing conditions of swellability so as to avoid degradation of the hydrocolloid. In this regard, instant specification on page 13, L 15-23 also states “The equilibrium swell of the cross-linked polymers of the present invention may range from 400% to 5000%, 400% to 3000%, 400% to 2000%, usually ranging from 400% to 1300%, preferably being from 500% to 1100%, depending on its intended use. Such equilibrium swell may be controlled by varying the degree of cross-linking, which in turn is achieved by varying the cross-linking conditions, such as the type of cross-linking method, duration of exposure of a cross-linking agent, concentration of a cross-linking agent, cross-linking temperature, and the like. “Thus, Wittwer similar to instant invention recognizes that swellability is a function of

granularity, temperature, specific material employed etc. Wittwer is directed to solving the same problem as that of the instant invention i.e., obtain equilibrium swell, avoid rapid degradation, and maintain the water content; and also suggests finite number of possibilities that may be optimized to attain instant swellable polymer. Thus, a skilled artisan would have been readily able to determine the conditions such as temperature, granularity, type of polymer, nature of crosslinking etc., in obtaining a hydrocolloid polymer with a predetermined amount of water, swellability and the degradation. Particularly, Wittwer suggests methods of obtaining higher quantities of water in the hydrocolloid and yet feel superficially dry such that they do not stick together (col. 3, L 1-10). The argument regarding fig. 1 is not persuasive because the teachings of the prior art are not limited to figures and examples and should be considered as a whole. One skilled in the art would be able to optimize the conditions so as to produce a hydrocolloid with desired amount of water (see claim 1 of Wittwer), even distribution of water within the granules, swellability and plasticity such that the final polymer does not degrade rapidly. For the argument regarding in vivo degradation, mere arguments without any evidence to show that the gelatin hydrocolloid gels do not degrade at the claimed rate are not persuasive.

The argument regarding free aqueous phase and swellability is not persuasive because Wittwer only teaches gels for injection molding and not the addition of any suspensions or carriers for such utility.

**Claims 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4482386 to Wittwer as applied to claims 1, 19, 21, 24, 29, 31, 32, 34 and 36 above, and further in view of US 4,124,705 to Rothman et al and US 4,515,637 to Cioca**.

Wittwer teaches gelatin or synthetic polymers that swellable and also suitable for injection molding to prepare shaped articles. Wittwer teaches natural and synthetic polymers are suitable for the preparation of injectable hydrocolloids, but fails to teach an active agent (claim 25) such as a clotting agent (claim 26) or thrombin.

Rothman et al (hereafter Rothman) discloses an agent for intravascular administration consisting of a suspension of minute particles of a polysaccharide that is blocks the finer blood vessels (abstract, lines bridging col. 1-2 and paragraph bridging col. 11-col. 12). The polysaccharide of Rothman is biodegradable and resorbable because Rothman describes that the hydrophilic swellable particles are broken down by alpha-amylase in the blood plasma (col. 2, l 4-16) and further, according to the instant claim 35, the ability to be resorbable is inherent to the polysaccharide of Rothman. Similarly, the ability to swell is a property inherent to the polysaccharides described by Rothman. Rothman teaches a size range of 0.1 to 300 microns (col. 5, L 18-36), which overlaps with the claimed range of 0.01 mm to 5 mm (10 microns-5000 microns). Rothman further describes that the polymeric gel particles are produced by disintegrating the larger pieces of gel, which reads on fragmented gel claimed in the instant (col. 8, L 3-14). With respect to the limitations of "single phase" and "substantially free form a free aqueous phase", Rothman does not teach including any

other substance or component in the polysaccharide suspension other than for the formation of the gel or the ability to form a gel, and also states that the gels contain more than 50% by weight water but less than 98%water (col. 4, L 58-70), which implies that the gels do not contain any free water. Rothman discloses that the particulate suspension is injected intravascularly (col. 8, L 31-48), in conjunction with a therapeutic (col. 9, L 25-34) or a diagnostic agent (col. 8, L 49 through col. 9, L 24). Further the particulate suspension containing polysaccharide particles (of Rothman) read on a single phase aqueous colloid and are swellable upon administration and hence the presence of aqueous solution (for suspending the particles) and hence read on the claimed “free from a free aqueous phase”. The therapeutic or diagnostic agents of Rothman read on instant claim 25 and particularly mention coagulation factors of claim 26 (col. 9, line 28-30). Rothman fails to teach the specific clotting agent, thrombin of claim 27, but teaches inclusion of clotting agents in the swellable gels for affecting coagulation.

Cioca teaches thrombin as an effective clotting factor for stoppage of bleeding locally (col. 2). Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to use swellable hydrocolloids of Wittwer containing gelatin polymer for delivering active agents such as coagulating factors to the desired site because Rothman suggests swellable hydrogels for delivering therapeutic agents such as coagulating agents. Further, it would have been obvious for a skilled artisan to include thrombin as a coagulation factor in the hydrogel composition of Wittwer with an expectation of achieving the desired clotting or coagulation.

***Response to Arguments***

Applicants' arguments of 7-29-09 are not persuasive. It is argued that neither Rothman nor Cioca teach the claimed equilibrium swell and hence do not remedy the deficiencies of Wittwer. However, the arguments are not persuasive because the arguments regarding swelling have been addressed above. Rothman and Cioca have been cited for the motivation to include an active agent in the product of Wittwer.

**Claims 30-32 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4482386 to Wittwer as applied to claims 1, 19, 21, 24, 29, 31, 32, 34 and 36 above, and further in view of US 4,124,705 to Rothman et al and US 6,129,761 to Hubbell OR Alternatively, Claims 31-32 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4482386 to Wittwer as applied to claims 1, 19, 21, 24, 29, 31, 32, 34 and 36 above, and further in view of US 6,129,761 to Hubbell .**

**In response to the amendment to claim 30, which now includes protein and polysaccharides, the scope of the claim 30 with respect to aqueous colloid is similar to that of claim 35. Hence, claim 30 is now rejected under the same statute as that of claim 35.**

Wittwer teaches gelatin or synthetic polymers that swellable and also suitable for injection molding to prepare shaped articles. Wittwer teaches natural and synthetic polymers are suitable for the preparation of injectable hydrocolloids, but fails to teach the combination with gelatin or other polymers, of instant claims.

Rothman, discussed above, teach polysaccharide swellable gels in combination with active agents or hydrocolloids comprising combinations of swellable polymers.

Hubbell teaches injectable hydrogel compositions useful for delivering cells or other bioactive agents via injection and thus provide engraftment and a 3-D template for new cell growth, custom molding of implants as well as implantation of tissues (abstract and col. 5, L 5-23) . The polymers of Hubbell include biodegradable, biocompatible hydrogels such as polylactides, polyanhydrides, polysaccharides and natural polymers such as gelatin, collagen, fibrin etc (col. 7-8), all of which described in the instant. Hubbell also teaches combination or mixtures of polymers (col. 8, L 63 –col. 9, L 12). It would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to combine other synthetic and natural swellable polymers of Rothman or Hubbell with the polysaccharide swellable polymers of Wittwer for administration because Wittwer suggests that protein as well synthetic polymers are suitable for preparing injection moldable articles, Rothman suggests polysaccharides and Hubbell suggests several swellable hydrogel polymers (both natural polymers such as gelatin and synthetic polymers) as well as their combinations for administering active agents to the localized or for tissue remodeling or preparing shaped moldable articles. Accordingly, a skilled artisan would have expected to be able to administer active agents or promote tissue engraftment with individual as well as mixtures of hydrogel polymers.

***Response to Arguments***

Applicants' arguments of 7-29-09 are not persuasive. It is argued that Hubbell fails to teach an equilibrium swell of 400 to 5000% and hence do not remedy the deficiency of Wittwer. Applicants' arguments regarding the teaching of an equilibrium swell of 400 to 5000% have been explained in the teachings of Wittwer. Since the arguments do not specifically address the teachings of Hubbell i.e., the combination of polymers, the rejection has been maintained.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611
November 22, 2009